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(71) Applicant *(for all designated States except US)*: UNIVERSITY COLLEGE CARDIFF CONSULTANTS LIMITED [GB/GB]; P.O. Box 923, Cardiff CF1 3TE (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: EDWARDS, Peter, Gerald [GB/GB]; 81 Plymouth Road, Penarth, South Glamorgan CF64 3DE (GB). FLEMING, James, Stephen [GB/GB]; University College Cardiff Consultants Limited, P.O. Box 923, Cardiff CF1 3TE (GB). LIYANNAGE, Sundantha, Susila, Lekam, Wasam [LK/GB]; University College Cardiff Consultants Limited, P.O. Box 923, Cardiff CF1 3TE (GB).

(74) Agents: STUART, Ian et al.; Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP (GB).



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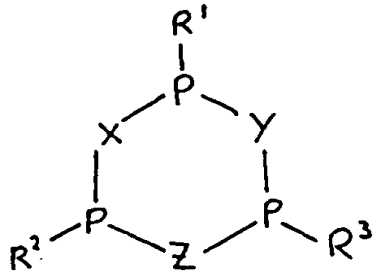
(54) Title: CYCLIC PHOSPHINES, PHOSPHINE OXIDES AND COMPLEXES THEREOF


(57) Abstract

The invention relates to processes for the preparation of phosphine derivatives, to certain novel phosphine derivatives obtainable by this process and to their uses, for example in catalysis. In particular, to a process for the preparation of a compound of formula (I) where $R^1$, $R^2$ and $R^3$ may be the same or different and are hydrogen, or optionally substituted hydrocarbyl or optionally substituted heterocyclyl groups; and X, Y and Z may be the same or different and are optionally substituted alkylene or arylene groups.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# CYCLIC PHOSPHINES, PHOSPHINE OXIDES AND COMPLEXES THEREOF.

The present invention relates to processes for the preparation of phosphine derivatives, to certain novel phosphine derivatives obtainable by this process and to their uses, for example in catalysis.

Alkyl and aryl phosphines are very important in transition metal chemistry as ligands that form complexes that have useful properties such as homogeneous catalysis.

Examples of the application of tertiary phosphines in catalysis include $(Ph_3P)_3RhCl$ otherwise known as Wilkinson's Catalyst, which catalyses the hydrogenation of alkenes, for example in the reaction.

$$RCH{=}CH_2{+}H_2 \rightarrow RCH_2CH_3$$

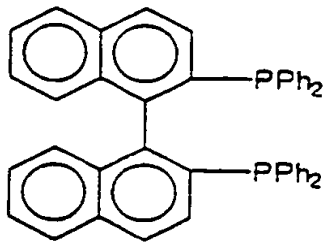
In addition, the carbonylation of methanol to produce acetic acid or acetate esters (depending upon reaction conditions) may be catalysed by rhodium diphosphine (1,2-bisdiphenylphosphinoethane) complexes.

There is a wide range of tertiary phosphine ligands known that contain one, two or more phosphorus donor atoms that can coordinate metals to form complexes. Particularly monodentate and bidentate phosphine ligands have been studied most intensively, the former are generally cheaper and easier to obtain and use. However, the latter offer advantages in some systems due to the enhanced stability of the complexes formed and their increased steric influence on the reactions that can subsequently be made to occur on the metal complex. Tertiary phosphine ligands are also important in applications of metal phosphine complexes in other fields such as for pharmaceutical and medical diagnostic purposes. Examples include certain gold anti-arthritic

drugs and the technetium heart imaging agents. In both of these cases, bidentate phosphine ligands are used which may also contain other pendant functions such as ether groups.

A feature of tertiary phosphines is their ability to carry a wide range of functionalities and for the substituent alkyl or aryl functions to be derivatised such that ancillary functions can be readily incorporated in positions both close to the phosphorus donor atom and at distances removed from it. This feature enables the phosphine ligand to be modified with considerable freedom, allowing manipulation of steric and electronic properties and the incorporation of further donor atoms of various types and with varying donor abilities. Thus stereochemical control and stabilisation of intermediates in reactions can be introduced to metal complexes and reaction systems greatly enhancing the performance of the complexes in various applications. For example, the functions on phosphorus can be designed to introduce chirality that in turn enables complexes of the chiral phosphine ligand to induce asymmetry (or chirality) into the product from achiral or prochiral substrates. An example of this is the l-Dopa synthesis with rhodium "BINAP" complexes of formula A:

A

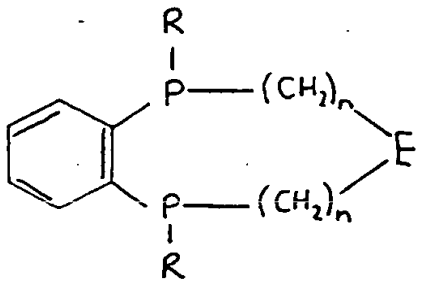



This variability of functionality can also be of benefit outside the direct influences on the reactivity of complexes. For example, incorporation of chosen functions can impart selective solubility (e.g. in water rather than organic solvents) or modify the complexes

formed from the phosphine ligand so as to favour lipophilicity etc. for specific applications in pharmaceutical and other biological areas as demonstrated by the use of tetrakis-ethoxyethyldiposphinoethane $[(CH_3CH_2OCH_2CH_2)_2PCH_2CH_2P(CH_2CH_2OCH_2CH_3)_2]$ as a ligand for technetium in a diagnostic heart imaging agent "Myoview".

Phosphorus macrocycles containing three donor atoms have been previously reported (Kyba et al, J. Amer. Chem. Soc. (1977) 99, 8053) which are based upon the 1,2-aryl backbone connecting two of the phosphorus atoms as shown as formula B:

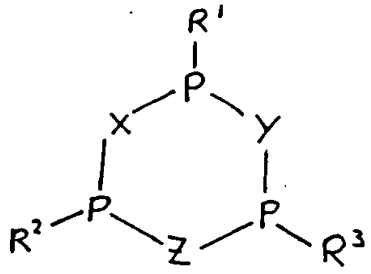
B




where E is O, S, NR, PR or AsR, R is alkyl or aryl and N is 2 or more. The linkages to the hetero atom E are aliphatic and of variable length. All these macrocycles were prepared by a "high dilution" method which is not stereospecific.

The present invention provides a process for the preparation of a compound of formula (I):

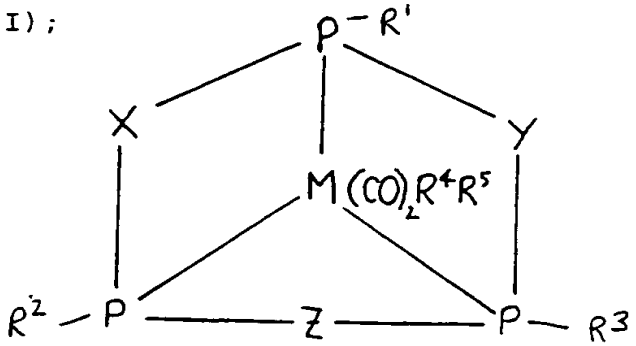
(I)




where $R^1$, $R^2$ and $R^3$ may be the same or different and are hydrogen, or optionally substituted hydrocarbyl or optionally substituted heterocyclyl groups; and

X, Y and Z may be the same or different and are optionally substituted alkylene or arylene groups; which process comprises either (a) reacting a compound of formula (II);

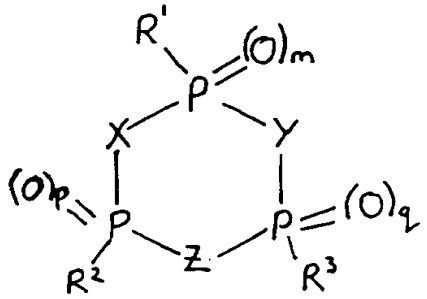
(II)



where $R^1$ , $R^2$ , $R^3$, X, Y and Z are as defined above, M is a metal, $R^4$ is halogen and $R^5$ is hydrogen or halogen; with a base; or optionally a metal scavenging agent such as EDTA or cyanides; or,

(b) by reducing a compound of formula (III);

(III)



where $R^1$ , $R^2$ , $R^3$, X, Y and Z are as defined above, and m, p and q are 0 or 1 provided that at least one of m, p or q is 1;

and optionally thereafter changing one or more of the groups $R^1$, $R^2$ and $R^3$ for other such groups. Compounds of formula (II) would be expected to adopt a chair like configuration hereinafter in particular in scheme 1 and scheme 2.

Suitable hydrocarbyl groups for $R^1$, $R^2$ and $R^3$ include alkyl, alkenyl, alkynyl or aryl. They may be normal

aliphatic, chiral or contain optional substituents.

Examples of optional substituents for said hydrocarbyl or heterocyclyl groups include aryl, halo such as fluoro, chloro, bromo or iodo, haloalkyl such as trifluoromethyl, hydroxy, acyl such as acetyl, nitro, amino or mono- or disubstituted amino when the substituents include alkyl, aryl, alkenyl or alkynyl, alkoxy groups, imino, acyl, carboxy or salts, esters or amides thereof such as alkyl esters. Other optional substituents include phosphino or mono- or di-substituted phosphino when the substituents include alkyl, aryl, alkenyl, alkynyl, alkoxy, amino, acyl, carboxy or salts, esters or amides thereof such as alkyl esters, phosphates or salts, phosphonates or esters, thiol, alcohol, ethers or thioethers when the substituents may be any of those above. It will be appreciated that the optional substituents may be chiral, for example, (+) or (-) menthol.

Preferably $R^1$, $R^2$ and $R^3$ are hydrogen or optionally substituted alkyl such as methyl or 2-propyl or t-butyl.

Most preferably $R^1$, $R^2$ and $R^3$ are all hydrogen or all alkyl, such as methyl, 2-propyl, or t-butyl.

Suitable groups X, Y and Z are optionally substituted trimethylene, tetramethylene or 1,2-phenylene, any of which may be optionally substituted by the groups listed above as potential substituents for $R^1$, $R^2$ and $R^3$ groups.

Suitably the metal M is chromium, molybdenum or tungsten.

Suitably $R^4$ and $R^5$ are fluorine, chlorine, bromine or iodine, preferably chlorine. When both $R^4$ and $R^5$ are chlorine, compounds of formula (I) are liberated directly and relatively less reduction to the precursor

tricarbonyl takes place. This is believed to be due to the enhanced stability of the +2 oxidation state in the chlorides as opposed to the bromides and iodides.

Suitable bases for use in reaction (a) are strong bases such as alkali metal hydroxides or alkoxides, in particular sodium hydroxide.

The reaction is suitably effected in a solvent, in particular aqueous or alcoholic solvents such as water or ethanol, or mixtures thereof. Temperatures in the range of from 0 to 100°C, conveniently between 0 and 25°C are employed. In this case, the preferred transition metal M is molybdenum.

Reduction of compounds of formula (III) can be carried out using standard methods, for example with lithium aluminium hydride or trichlorosilane according to established procedures (see "Organic Phosphorus Compounds", Volume1, by GM Kosolapoff and C Maier, J Wiley, New York 1972).

As used herein, the term 'alkyl' includes straight or branched chain alkyl groups, suitably of from 1 to 10 carbon atoms. Similarly the terms "alkenyl" and "alkynyl" refer to unsaturated straight or branched chains, for example of from 2 to 10 carbon atoms. The term 'aryl' includes aromatic rings such as phenyl or naphthyl and which may carry further substituents such as halogens (F, Cl, Br, I), ethers, amines, phosphines, carboxy or salts or esters or amides, sulphonate or salts or esters, phosphate or phosphonate or salts or esters. The terms " alkylene" and "arylene" refer to divalent alkyl chains or aryl rings respectively. In addition the term "heterocyclyl" includes rings containing for example up to 10 ten ring atoms, up to four of which may be selected from oxygen, sulphur or nitrogen.

Reaction (a) above provides a high yielding process which is much easier to carry out than prior art processes for the preparation of tertiary phosphine macrocycles. Yields of from 75% to quantitative yields have been achieved using this process.

Furthermore, compounds obtained using reaction (a) above are stereospecific. In particular, all three lone pairs of electrons on the phosphorus atoms are on the same side of the molecule. These compounds are known as syn-syn isomers.

This is the first time such stereospecific tertiary phosphine derivatives have been prepared and these compounds form a further aspect of the invention.

Thus the invention further provides a compound of formula (I), wherein $R^1$, $R^2$, $R^3$, X, Y and Z are as defined above and wherein all lone pairs are orientated on the same side of the ring structure.

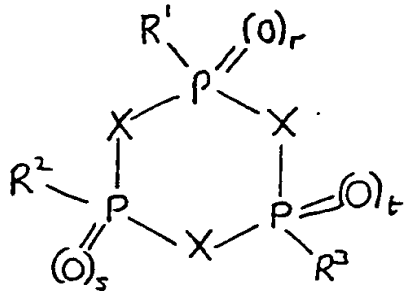
The syn-syn isomers can be converted to syn-anti isomers by heating or by deprotonating (with base) the syn-syn isomers (free of metal) where R=H followed by reprotonation, or by alkylating the syn-syn isomer where R=H with alkyl halides, or by hydrophosphination (insertion of alkene in the P-H bond).

The syn-syn isomer where R-isopropyl and the phosphorus atoms are linked by trimethylene is converted to syn-anti by heating in mesitylene solvent at 156°C. The half-life for conversion is 20 hours.

A further preferred group of compounds of formula (I) are those where X, Y and Z are all the same. This is the first time that such compounds have been prepared. Thus in a further aspect, the invention provides a compound of

formula (IV) :

(IV)



where $R^1$, $R^2$, $R^3$, and X are as defined above and r, s and t are independently selected from 0 or 1.

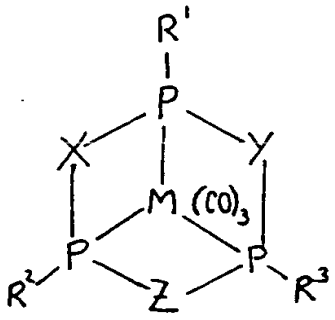
Symmetrical compounds of formula (II) are advantageous when such compounds are used in the subsequent synthesis of metal compounds derived from the free macrocycles and in the minimisation of unwanted isomeric products of the metal complexes prepared and of the macrocycles themselves. Thus, they simplify the coordination chemistry of derived complexes which are also easier to study, analyse, purify and isolate due to the reduced complexity of the derived complexes and the reduced likelihood of obtaining mixture of isomers. They also simplify the properties of the derived complexes and maximise the likelihood of the macrocycle binding to only one metal atom with all three phosphorus donors, hence minimising other possible interactions and coordination modes (eg such as a bridging configuration with two phosphorus atoms bonded to one metal and one to another which could lead to polymeric, intractable materials).

The optional replacement of one group $R^1$, $R^2$ or $R^3$ with other such groups may be carried out by the skilled chemist using conventional methods. For instance, a range of functional groups may be incorporated either directly onto the phosphorus atom or within substituents in the group using conventional techniques.

In one such reaction, a compound of formula (I) wherein $R^1$, $R^2$ and $R^3$ are all hydrogen are alkylated. If present, the above-mentioned stereospecificity may however be altered at this stage and the alternative isomer or tritertiary phosphine macrocycle (i.e. with two lone pairs pointing in one direction away from the plane of the macrocycle and one lone pair pointing in the other direction) may be obtained.

Compounds of formula (II) are suitably prepared by reaction of a compound of formula (V):

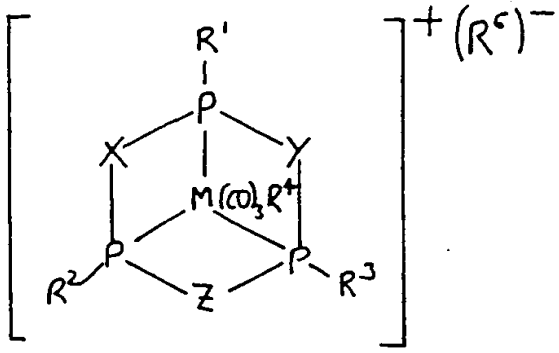
(V)




where $R^1$, $R^2$, $R^3$, M, X, Y and Z are as defined above; with a halogenating agent, such as halogen for example chlorine. Suitable reactions conditions for the halogenation would be apparent to the skilled chemist.

This reaction may give rise initially to a salt of the metal complex of formula (VI) in formal oxidation state +2:

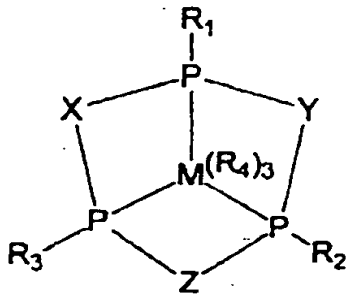
(VI)



where $R^1$, $R^2$, $R^3$,$R^4$, M, X, Y and Z are as defined above and $R^6$ is halide ion. Salts of formula (VI) are typically contaminated with neutral dihalide complex and can be converted quantitatively to the compound of formula (II) where $R^5$ is halide by stirring as a suspension or solution in a suitable solvent such as dichloromethane or ethanol.

Depending upon the nature of the metal M and the substituents $R^1$, $R^2$ and $R^3$; a compound of formula (V) may react with halogens (chlorine, bromine or iodine) to give a trihalide metal complex of formula (VIb) where $R^4$ is halide and where the metal is in oxidation state +3 and from which the macrocycle may also be liberated stereospecifically (as the syn-syn isomer) to give a compound of formula (I) and by the same method as described previously (example 11) by action of base (such as sodium hydroxide or alkoxide) or metal scavanging agent (such as EDTA or cyanide).

(VIb)




Compounds of formula (V) where $R^1$, $R^2$ and $R^3$ are all hydrogen may be converted to the corresponding alkyl derivatives at this time using the procedures described by Coles et al., J. Chem Soc. Dalton Transactions, (1995) 1139.

Suitable compounds of formula (V) where X, Y, and Z are $C_3H_6$ have been identified by their analytical data. Examples are given in the table below.

TABLE NMR, IR and Analytical Data for $[M(CO)_3$*cyclo*$-(RPC_3H_6)_3]$

| Complex / Method | $\delta$ $^{31}P^a$ | $\nu(CO)^c$ | %C found (calc) | %H found (calc) |
|---|---|---|---|---|
| $[Mo(CO)_3$*cyclo*$-(\{(CH_3)_2CHPC_3H_6\}_3]$ / A | 10.1 | 1915, 1813 | 47.6 (48.3) | 7.80 (7.40) |
| $[Mo(CO)_3$*cyclo*$-(TMSMPC_3H_6)_3]^c$/ A | 3.5 | 1923, 1828 | 42.2 (43.6) | 8.15 (7.30) |
| $[Mo(CO)_3$*cyclo*$-(CH_3PC_3H_6)_3]$ / A | -8.6 | 1920, 1827 | 40.1 (40.5) | 5.65 (6.15) |
| $[Mo(CO)_3$*cyclo*$-(C_6H_5CH_2PC_3H_6)_3]$ / A | 2.6 | 1922, 1821 | 58.9 (58.2) | 5.86 (5.99) |
| $[Mo(CO)_3$*cyclo*$-(C_3H_5PC_3H_6)_3]$ / A | -1.4 | 1926, 1834 | 47.6 (46.5) | 6.00 (6.40) |
| $[Mo(CO)_3$*cyclo*$-(CH_3CH_2PC_3H_6)_3]$ / B | 4.4 | 1918, 1815 | 44.9 (45.0) | 6.79 (7.51) |
| $[Mo(CO)_3$*cyclo*$-(\{CH_3\}_2CHCH_2PC_3H_6)_3]$ / B | 5.2 | 1920, 1828 | 50.2 (50.2) | 7.89 (8.33) |
| $[Cr(CO)_3$*cyclo*$-(CH_3PC_3H_6)_3]$ / A | 16.4 | 1911, 1813 | 45.1 (45.0) | 6.89 (6.75) |
| $[Cr(CO)_3$*cyclo*$-(CH_3CH_2PC_3H_6)_3]$ / B | 23.6 | 1911, 1813 | 48.2 (48.9) | 7.06 (7.47) |
| $[Cr(CO)_3$*cyclo*$-(\{CH_3\}_2CHCH_2PC_3H_6)_3]$ / B | 23.9 | 1911, 1822 | 55.0 (54.8) | 8.32 (8.55) |
| $[Cr(CO)_3$*cyclo*$-(CH_3OC_3H_6PC_3H_6)_3]$ / B | 22.2 | 1911, 1806 | 49.8 (50.2) | 8.09 (7.84) |
| $[Cr(CO)_3$*cyclo*$-(C_2H_5OC_2H_4PC_3H_6)_3]$ / B | 20.9 | 1908, 1813 | 50.2 (50.2) | 7.84 (7.84) |
| $[Cr(CO)_3$*cyclo*$-(NH_2C_3H_6PC_3H_6)_3]$ / B | 22.1 | 1911, 1806 | 47.2 (47.6) | 7.84 (7.93) |
| $[Cr(CO)_3$*cyclo*$-(CH_3SC_3H_6PC_3H_6)_3]$ / B | 22.3 | 1904, 1813 | 46.5 (46.3) | 7.25 (7.26) |
| $[Cr(CO)_3$*cyclo*$-(Ph_2PC_3H_6PC_3H_6)_3]$ / B | 22.5[e] | 1918, 1822 | 67.3 (66.0) | 6.60 (6.37) |

a) $\delta$ ppm relative to $H_3PO_4$ ($\delta$ = 0); b) Hz, c) TMSM = $Me_3SiCH_2$ ; d) Nujol mull; e) -17.4 for pendant phosphine.

The macrocycle complexes in the Table may be prepared by either of the following methods.

Method A:

$$(H_3P_3mac)M(CO)_3 \xrightarrow{\text{(i) 3BuLi (ii) 3RX}} (R_3P_3mac)M(CO)_3$$

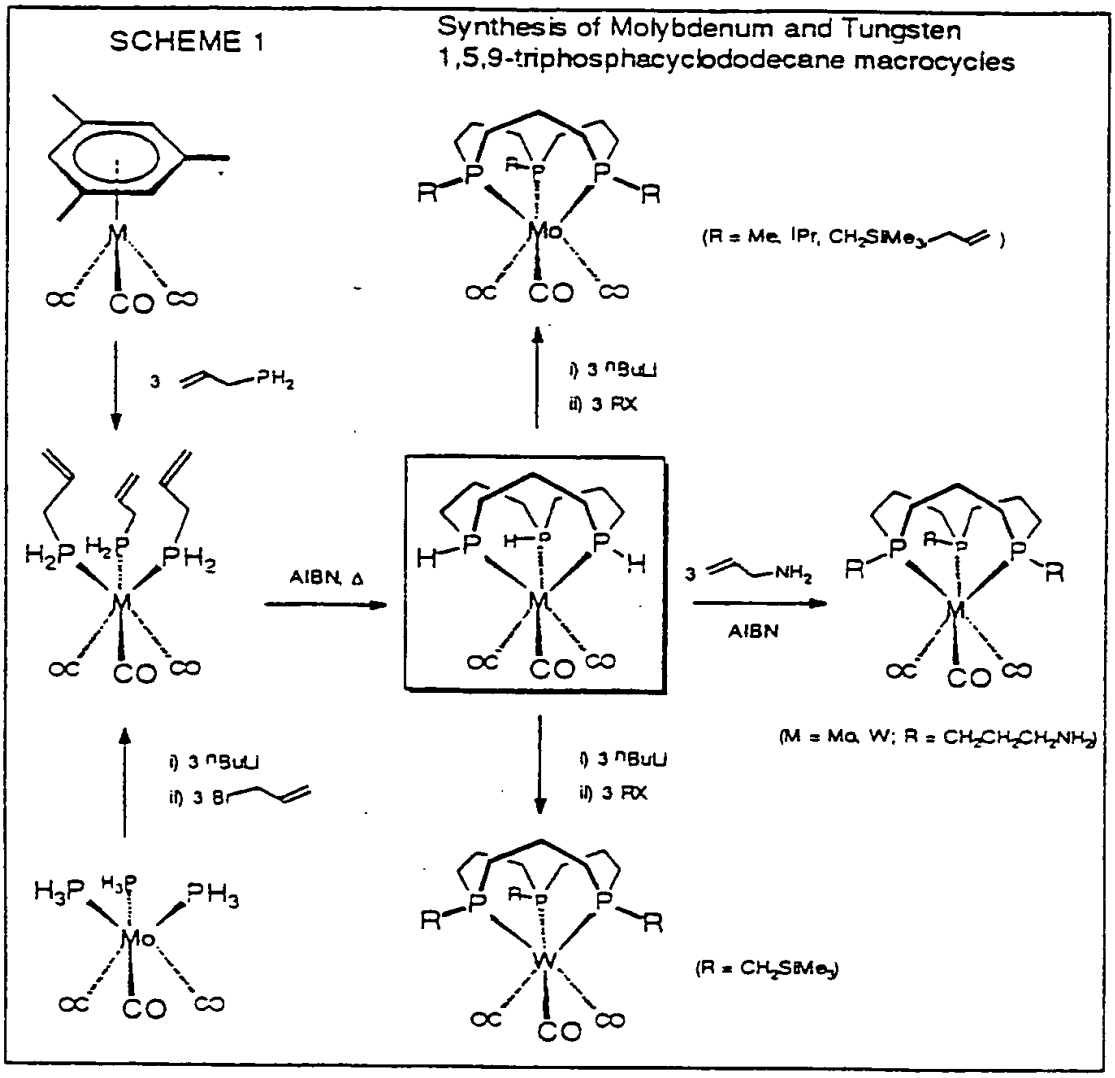
(R = alkyl, X = halide, M = Mo, Cr)

Method B:

$$(H_3P_3mac)M(CO)_3 \xrightarrow{\text{excess } \swarrow\!\!\!\!\searrow R,\ \text{AIBN}} (R'_3P_3mac)M(CO)_3$$

(R = H, alkyl, ether, thioether, amine, phosphine; R' = $CH_2CH_2R$; M = Mo, Cr)

A typical scheme for the preparation of a compound of formula (V) is set out in Scheme 1 below.



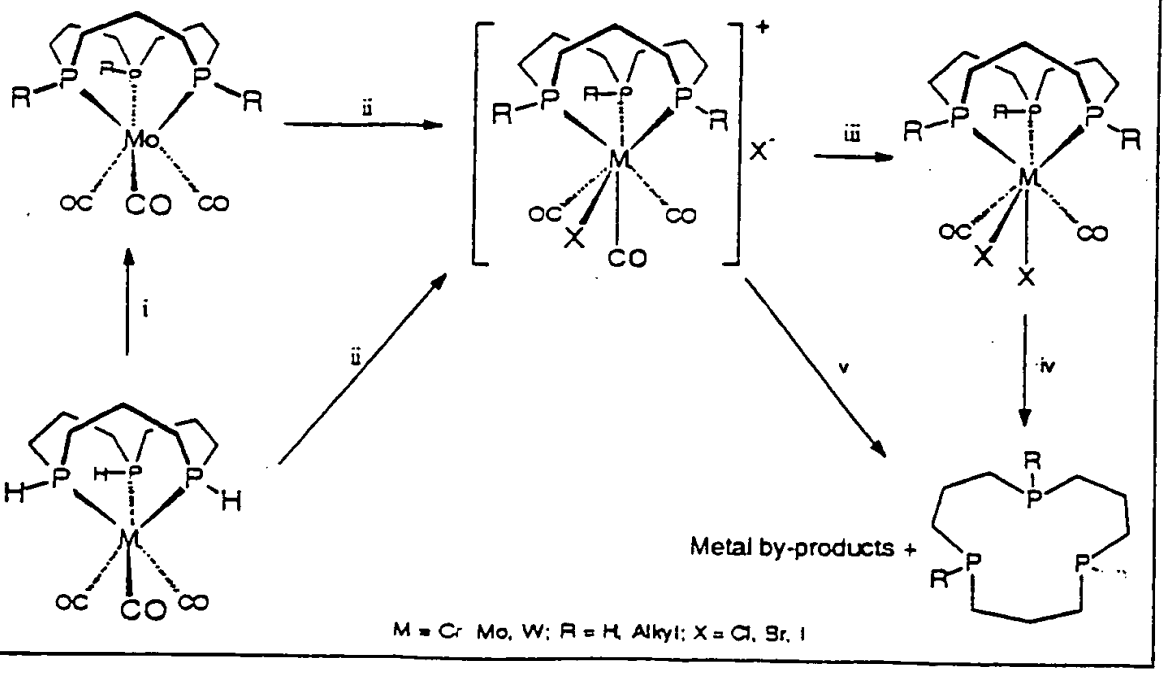
Compounds of formula (III) above are novel and form a further aspect of the invention. They may be useful in their own right as metal scavengers.

Compounds of formula (III) as well as compounds of formula (IV) where r, s and t are 1 are suitably prepared by oxidation of a compound of formula (V) as defined above.

Suitable oxidising agents for use in the reaction include hydrogen peroxide, oxygen or ozone. The reaction is suitably effected in a solvent such as an organic solvent, for example toluene, at moderate temperatures, for example of from 0 to 100°C, depending upon the nature of the oxidising reagent and the solvent employed. A particularly suitable metal ion M in this case is chromium.

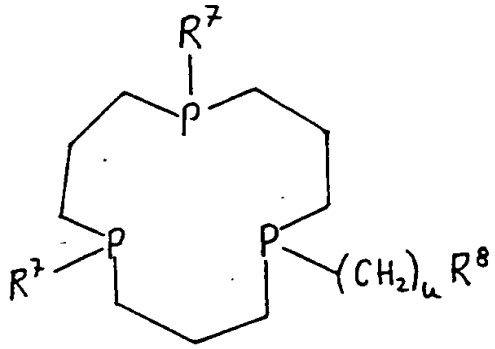
Some compounds of formula (V) are known compounds and may be prepared using published techniques (Coles et al., supra). A particularly preferred route for the preparation of compounds of formula (I) is illustrated using preferred trimethylene set out in Scheme 2 below.

Scheme 2: i) $3^{n}BuLi$, 3RX (THF); ii) $X_2$ ($CH_2Cl_2$); iii) $CH_2Cl_2$ 2/3 days



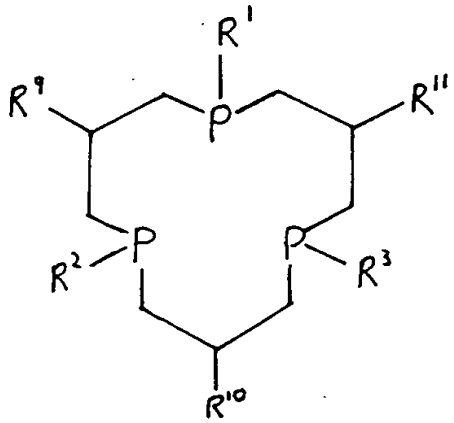
A feature of this scheme is that the alkylation reactions from the secondary phosphine macrocycles to the tertiary phosphine macrocycles are stepwise. This enables selective incorporation of substituents on phosphorus and the potential for incorporation of other functions on only one phosphorus atom (or two) for example as in Formula (VII):

(VII)



where $R^7$ and $R^8$ are various groups as set out above for $R^1$ $R^2$ or $R^3$ and can contain hetero atoms and $u \geq 1$). In addition, it is possible by this route to prepare triphosphorus macrocyclic ligands with functions on the trimethylene bridges between the phosphorus atoms by starting with, and cyclising, the appropriate primary alkenyl phosphine metal complex of formula (VIII):

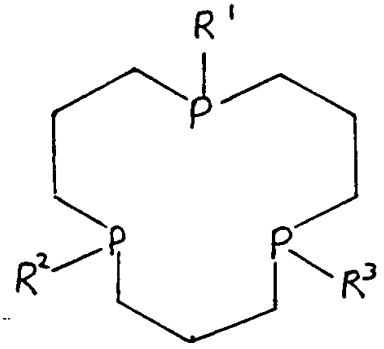
(VIII)



where $R^1$, $R^2$ and $R^3$ are as defined above and $R^9$, $R^{10}$ and $R^{11}$ are for instance optical substituents as described above. These functions can also include other heteroatoms and organic functions. This route is also applicable to bridging functions other that the

trimethylene unit, e.g. by cyclising the butenylphosphine complexes (analogous to the allylphosphine complexes), the fifteen membered triphosphorus macrocycle with four carbon bridges between the phosphorus atoms can be prepared of formula IX:

(IX)




where $R^1$, $R^2$ and $R^3$ are as defined above. This macrocyclic system may also be derivatised either at phosphorus or on the backbone linking the phosphorus atoms. By appropriate choice of the alkenylphosphine, the functions appended to the backbone linkages can be placed selectively in various positions (i.e. can be adjacent to or more distant from the phosphorus atoms).

The method of the invention provides a means of liberation of the free, uncoordinated macrocyclic ligands. This has never before been achieved and allows the ligands to be coupled to (in principle) any other metal and for other purposes where the free uncoordinated macrocycle is required (e.g. as a scavenging or complexing agent).

Compounds of formula (I) potentially applicable in a number of ways principally because the enhanced stability of complexes formed from the macrocycle (over that of mono and bidentate ligands) will be of great value. For example, catalyst degradation reactions (which are amongst the major problems encountered in homogeneous catalysis with mondentate phosphines) can be inhibited or even completely stopped and metabolism of agents for

biological and medical use can also be inhibited allowing the drug to reach the desired site of activity more reliably.

Compounds of formula (I) and (II) may be used to make a wide range of metal complexes for catalyst use. Examples of metals which may be included in such complexes include transition elements in the Fe, Co and Ni triads, of use in catalytic hydrogenations and carbonylations; metals of the Cu triad, for the influence on oxidation and reduction behaviour that may be of interest in the modelling of metalloenzymes, metals in the Ti and V triads for use in alkene oligomerisations and polymerisations and metals in the V, Cr, and Mn triads for the investigation of other reactions of alkenes such as alkene metatheses. Essentially, any catalytically useful metal (of which many are known) may be complexed with the free phosphine compound. Further examples include tin, nickel or lanthanides such as ytterbium and lutetium. Since the alkyl/aryl substituent $R^1$, $R^2$ or $R^3$ on the phosphorus atoms can be chiral, this may influence catalytic and stoichiometric reactions of prochiral substrates and so give rise to catalysts useful in chiral induction (e.g. in catalytic hydrogenations). This feature of chirality may also be used in catalytic polymerisation and oligomerisation reactions in controlling tacticity and number average molecular weights in the polymer/oligomer products. It has been found that the macrocycles may be reacted with a variety of metal compounds and in a range of solvents, whereby new macrocycle complexes are readily prepared. Examples are in Equations 2, 3, and 4. These procedures can in principle be applied to the preparation of $12aneP_3R_3$ complexes of any metal.

Eq. 2: $TiCl_4 + 12aneP_3R_3 \rightarrow 12aneP_3R_3.TiCl_4$

Eq. 3: $FeCl_2 + 12aneP_3R_3 \rightarrow 12aneP_3R_3\text{-}FeCl_2$

Eq. 4: $[Rh(C_2H_4)_2Cl]_2$ + 12aneP$_3$R$_3$ → 12aneP$_3$R$_3$RhCl

Thus the invention further provides a catalyst which comprises a complex containing a compound of formula (I) as hereinbefore defined.

The following Examples illustrate the invention.

**EXAMPLE 1**

1) Preparation of 1,5,9-tris (2-propyl) triphosphacyclododecane [cyclo-$(\{CH_3\}_2CHPC_3H_6)_3$] (1)

a. A suspension of $[MX_2(CO)_2$cyclo-$(\{CH_3\}_2CHPC_3H_6)_3]$ (0.30 mmol; M=Mo, W; X = Cl, Br, I) in ethanol (30 cm$^3$) was stirred at room temperature for 16 hours. The mixture was cooled to 0°C and a large excess of NaOH pellets (>1.0g) added. The mixture was allowed to warm to room temperature and stirred for a further 4 hours. The solvent was removed in vacuo to give an oily grey residue. The mixture was cooled to 0°C and $H_2O$ (30 cm$^3$) was added and the mixture allowed to warm to room temperature and stirred for 1 hour. The product was extracted with petroleum ether 40-60° (3 x 50 cm$^3$). The combined organic phases were dried over $MgSO_4$ overnight. The $MgSO_4$ was removed by filtration and the solvent removed in vacuo to give (1) as a white solid (0.22 mmol, 75%).

b. A solution of $[MX_2(CO)_2$cyclo-$(\{CH_3\}_2CHPC_3H_6)_3]$ (0.30 mmol; M=Mo, W; X = Cl, Br, I) and KCN (>1.0g) in dimethylsulphoxide (50 cm$^3$) was heated to 100°C for 2 hours.

The mixture was allowed to cool and solvent removed in vacuo and the product was extracted in petroleum ether 40-60°C (3 x 50 cm$^3$). The combined organic phase was

washed with degassed water (2 x 50 $cm^3$) and dried with $MgSO_4$. The solvent was removed in vacuo to give (1) as a white solid (0.12 mmol, 40%).

NMR spectroscopy data (in $CDCl_3$ solution); $^{31}P\{^1H\}$ NMR - 19.8 p.p.m. (s); $^1H$ NMR 1.74 ppm (br m, $PCH_2CH_2$), 1.56 p.p.m. (7 line m, PCH), 1.42 p.p.m. (br m $PCH_2$), 0.99 ppm (dd, $^3J_{PH}$ & $^1J_{HH}$= 15 & 7 Hz, $CH_3$); $^{13}C\{^1H\}$ NMR 25.7 p.p.m. (dd, $^1J_{PC}$ = 17, $^3J_{PC}$ = 8 Hz, $PCH_2$), 24.3 ppm (D, $^1J_{PC}$ = 8 Hz, PCH), 19.6 ppm (s, $CH_3$), 19.4 ppm (br s, $PCH_2CH_2$). Mass Spec data (selected); 349 ($M^+$, 9% 305 (M-($C_{37}$)+ 38 %), 263 (M-$C_3H_7)_2^+$, 35%, 219 (M-$(C_3H_7)_3^+$, 27 %), 132 $CH_2P(CH_2)_3PCH_2$, 96%), 103 ($P(CH_2)_3P$, 100%). M.p. 114.8-115.3°C.

c. A solution of $[Mo(CO)_3$ *cyclo*-$(\{CH_3\}_2CHCPC_3H_6)_3]$ (0.30mmol) in 1,1,1-trichloroethane (50$cm^3$) was heated to 75°C and a solution of $X_2$ (0.30mmol, X = Br, I) in 1,1,1-trichloroethane (50$cm^3$) was added dropwise over 1h. The mixture was then heated at reflux temperature for 16h. The mixture was allowed to cool to room temperature and solvent removed *in vacuo* to give an oily, orange brown (for X = Br) or purple-brown (X = I) residue. A suspension of this residue in ethanol (30$cm^3$) was stirred at room temperature for 16h. The mixture was cooled to 0°C and a large excess of NaOH pellets (> 1.0g) added. The mixture was allowed to warm to room temperature and stirred for a further 4h. The solvent was removed *in vacuo* to give an oily grey residue. The mixture was cooled to 0°C and deoxygenated $H_20$ (30$cm^3$) was added and the mixture allowed to warm to room temperature and stirred for 1h. The product was extracted with petroleum ether 40-60°C (3 x 50$cm^3$). The combined organic phases were dried over $MgSO_4$ overnight. The $MgSO_4$ was removed by filtration and the solvent removed *in vacuo* to give (1) as a white solid (45%).

d. An identical method to (c) was employed with 1,1,2-trichloroethane rather than 1,1,1-trichloroethane used as solvent. However, the reaction was not stereospecific and a mixture of isomers of (1) were formed.

**EXAMPLE 2**

Preparation of 1,5,9-tris (trimethylsilymethyl)triphosphacyclododecane [cyclo-$(\{CH_3\}_3SiCH_2PC_3H_6)_3$] (2)

The method of Example 1 was used but with $[MoX_2(CO)_2$(cyclo $(\{CH_3\}_3SiCH_2PC_3H_6)_3]$ as the starting material.

NMR spectroscopy data; $^{31}P\{^1H\}$NMR-41.3 ppm. (s); $^1H$ NMR 1.71 ppm (6 line m, $PCH_2CH_2$), 1.41 ppm (m, $PCH_2CH_2$), 0.56 ppm (d, $^2J_{PH}$ = 2.1 Hz, $PCH_2Si$), 0.06 ppm (s, Si $CH_3$); $^{13}C\{^1H\}$ NMR 30.2 ppm (dd $^1J_{PC}$ = 17 Hz $^3J_{PC}$ = 9 Hz, $PCH_2CH_2$), 19.1 ppm (t, $^2J_{PC}$ = 6 Hz, $PCH_2CH_2$), 13.4 ppm (d, $^1J_{PC}$ = 29 Hz, $PCH_2Si$), 0.8 ppm (s, Si, $CH_3$).

**EXAMPLE 3**

Preparation of 1,5,9-tris(methyl)triphosphacyclododecane [cyclo-$CH_3PC_3H_6)_3$] (3)

The identical method of Example 1 was used but with $[MoX_2(CO)_2$(cyclo-$(CH_3PH_3H_6]$ as the starting material.

NMR spectroscopy data; $^{31}P\{^1H\}$NMR-45.7 ppm.

**EXAMPLE 4**

Preparation of 1,5,9-tris (benzyl)triphosphacyclododecane [cyclo-$C_6H_5CH_2PC_3H_6)_3$] (4)

The identical method of Example 1 was used but with $[MoX_2(CO)_2$(cyclo-$(C_6H_5CH_2PC_3H_6)_3]$ as the starting material.

NMR spectroscopy data; $^{31}P\{^1H\}$NMR-28.4 ppm.

**EXAMPLE 5**

Preparation of 1,5,9-tris(ally)triphosphacyclododecane [cyclo-$(c_3H_5PC_3H_6)_3$] (5)

The method of Example 1 was used but with $\{MoX_2(CO)_2(cyclo\text{-}(C_3H_5PC_3H_6)_3\}$ as the starting material. NMR spectroscopy data; $^{31}P\{^1H\}$NMR-36.7 ppm.

**EXAMPLE 6**

Preparation of 1,5,9-tris(ethyl)triphosphacyclododecane [*cyclo*-$(CH_3CH_2PC_3H_6)_3$] **(6)**.

The identical method of Example 1 was used but with [$MoX_2(CO)_2$*cyclo*-$(CH_3CH_2PC_3H_6)_3$]as starting material.

NMR spectroscopy data; $^{31}P\{^1H\}$NMR -31.7 ppm(s); $^1H$ NMR 1.72 ppm (7 line m, $PCH_2CH_3$, 1.52 ppm (7 line m, $PCH_2CH_2$) 1.36 ppm (7 line m, $PCH_2CH_2$), 1.02 ppm (dt, $^3J_{PH}$ 16 Hz & $^2J_{HH}$ 8Hz, $PCH_2CH_3$); $^{13}C\{^1H\}$NMR 27.7 ppm (dd, $^1J_{PC}$ 17Hz & $^3J_{PC}$ 9Hz, $PCH_2CH_2$), 19.2 ppm (m, $PCH_2CH_2$), 19.0 ppm (d, $^1J_{PC}$ 14Hz, $PCH_2CH_3$), 10.1 ppm (d, $^2J_{PC}$ 8Hz, $PCH_2CH_3$). Mass spec data (selected) 306 ($M^+$, 8%), 277 ($M\text{-}C_2H_5^+$, 100%).

**EXAMPLE 7**

Preparation of 1,5,9-tris(2-butyl)triphosphacyclododecane [*cyclo*-$(\{CH_3\}_2CHCH_2PC_3H_6)_3$] **(7)**.

The identical method of Example 1 was used but with [$MoX_2(CO)_2$*cyclo*-$(\{CH_3\}_2CHCH_2PC_3H_6)_3$ as starting material.

NMR spectroscopy data; $^{31}P\{^1H\}$ NMR -40.8 ppm (s); $^1H$ NMR 1.70 ppm (7 line m, $PCH_2CH_3$, 1.52 ppm (7 line m, $PCH_2CH$) 1.37 ppm (7 line m $PCH_2CH_2$), 1.27 ppm (dd, $^2J_{PH}$ 7Hz & $^2J_{HH}$ 3Hz, $PCH_2CH$), 0.95 ppm (d, $^3J_{PH}$ 3Hz, $CH_3$); $^{13}C\{^1H\}$ NMR 37.0 ppm (d, $^1J_{PC}$ 12Hz, $PCH_2CH$), 27.5 ppm (dd, $^1J_{PC}$ 16Hz & $^3J_{PC}$ 9Hz, $PCH_2CH_2$), 26.3 ppm (d, $^2J_{PC}$ 9Hz, $PCH_2CH$), 24.3 ppm (d, $^3J_{PC}$ 9Hz, $CH_3$)19.2 ppm (dd, $^2J_{PC}$ 8Hz & 6Hz, $PCH_2CH_2$). Mass spec data (selected) 391 ($M^+$, 15%), 333 ($M\text{-}C_4H_9^+$, 100%).

**EXAMPLE 8**

Preparation of macrocycle phosphonium salt [cyclo-

$(R\{H\}PC_3H_6)_3]^{3+}$ R = 2-propyl (8) trimethylsilymethyl (9), methyl (10), benzyl (11), allyl (12)).

To a cooled (-20°C) solution of cyclo-$(R\{H\}PC_3H_6)_3$ in diethyl ether (30 $cm^3$), a dried stream of Hcl gas in nitrogen was bubbled through the solution, immediately forming a white precipitate. When formation of the white precipitate had ceased, addition of Hcl was stopped and nitrogen was bubbled through the solution to purge the solution of excess Hcl. The white product was filtered off and washed with diethyl ether (3 x 10 $cm^3$).

$^{31}P\{^1H\}$ NMR data (in $CDOD_3$)

R = (8) 2 propyl, 21.1 ppm
(9) trimethylsilymethyl, 6.0 ppm
(10) methyl - 0.50 ppm
(11) benzyl - 14.3 ppm
(12) allyl - 6.1 ppm
(13) isobutyl, 4.0 ppm
(14) ethyl, +13.1
(15) methoxypropene, +12.5
(16) ethoxyethene, +10.7

Preparation of Trisecondary-trihydrochloride (17).

To degassed aqueous hydrochloric acid (10 $cm^3$, 10 M) was added 1,5,9-triphosphacyclododecane (0.30 mmol) at ambient temperature and the mixture stirred (2 hours), during which time the aqueous insoluble trisecondary phosphine had dissolved. The colourless solution was evaporated to dryness *in vacuo* leaving a white solid which was washed with diethyl ether and identified by $^{31}P$ NMR spectroscopy, yield: quantitative; $\delta_p$ ($CD_3OD$, 360.13 MHZ), -23.7(t) ($^1J_{PH}$ = 522 Hz).

**EXAMPLE 9**

Preparation of macrocycle phosphine oxides [cyclo-

$R\{O\}PC_3H_6)_3]$ (R = 2-propyl (18) trimethylsilymethyl (19), methyl (20), benzyl (21), allyl (22)).

a. A solution of cyclo-$(RPC_3H_6)_3$ in toluene (20 $cm^3$) was left exposed to air for 2 weeks.

For R=H (23); +31.3 $^1J_{PH}$ = 453; ethyl (24) +40.3; *syn-anti* ethyl (25), +42.9(t), +38.3(d) ($^4J_{P-P}$ = 60 Hz); isobutyl (26), 46.5; methoxypropene (27), 43.1; ethoxyethyl (28), +40.3; *syn-anti* methyl (29), +46.6(t), +40.6(d) ($^4J_{P-P}$ = 66 Hz); *syn-anti* $^t$butyl (30), +65.0(t), +58.6(d) ($^4J_{P-P}$ = 65 Hz); for R = allyl: 31.7, R = benzyl: 44.8.

b. A solution of $[Mo(CO)_3$cyclo-$(RPC_3H_6)_3]$ (0.10 mmol) in $CH_2Cl_2$ (30 $cm^3$) was cooled to 0°C and a stream of ozone in air (approx. 5%) was bubbled through the solution for 10 mins. Nitrogen was bubbled through the solution to purge the solution of ozone and then solvent was removed in vacuo to give an off-white solid. A suspension of this product in ethanol (30 $cm^3$) was stirred at room temperature for 16 hours. The mixture was cooled to 0°C and a large excess of NaOH pellets (>1.0g) added. The mixture was allowed to warm to room temperature and stirred for a further 4 hours. Solvent was removed in vacuo to give an oily grey residue. The mixture was cooled to 0°C and $H_2O$ (30 $cm^3$) was added and the mixture allowed to warm to room temperature and stirred for 1 hour. The product was extracted with petroleum ether 40-60°C (3 x 50 $cm^3$). The combined organic phases were dried over $MgSO_4$ overnight. The $MgSO_4$ was removed by filtration and the solvent removed in vacuo to give cyclo-$(R\{O\}PC_3H_6)_3$ as a white solid.

c. A solution of $[Mo(CO)_3$cyclo-$RPC_3H_6)_3]$ (0.10 mmol) in toluene (30 $cm^3$) was refluxed with $H_2O_2$ solution (30% w/v) for 48 hours. During this time a blue solid was formed. Solvent was removed in vacuo to give a blue solid. A

suspension of this product in ethanol (30 $cm^3$) was stirred at room temperature for 16 hours. The mixture was cooled to 0°C and a large excess of NaOH pellets (>1.0g) added. The mixture was allowed to warm to room temperature and stirred for a further 4 hours. Solvent was removed in vacuo to give an oily grey residue. The mixture was cooled to 0°C and $H_2O$ (30 $cm^3$) was added and the mixture allowed to warm to room temperature and stirred for 1 hour. The product was extracted with petroleum ether 40-60° (3 x 50 $cm^3$). The combined organic phases were dried over $MgSO_4$ overnight. The $MgSO_4$ was removed by filtration and the solvent removed in vacuo to give cyclo $(R\{O\}PC_3H_6)_3$ as a white solid. For R = 2-propyl, $\delta$ $^{31}P$=54.3 ppm, selected mass spectral data, 397 amu ($M^+$, 20%); for R = trimethylsilylmethyl, $\delta$ $^{31}P$ = 46.0 ppm.

**EXAMPLE 10**

1,5,9-triphosphacyclododecane was liberated from the Cr(II) precursor complex $(CrX_2(CO)_2$cyclo-$(HPC_3H_6)_3)$ (x = Cl, Br, I) using methods similar to those described for the molybdenum complexes above. Thus, stirring a suspension of $[CrX(CO)_3$cyclo-$(HPC_3H_6)_3]X$ in ethanol dichloromethane, or similar halogenated solvent results in the conversion into the neutral dihalo complex. This mixture was then treated with aqueous sodium hydroxide and stirred until digestion (of the Cr(II) complex was complete, typically 12h) and extracted with diethyl ether. The organic phase was separated, dried ($MgSO_4$) and evaporated to give the free macrocycle product (1,5,9-triphosphacyclododecane) as a colourless greasy solid in 40% yield. NMR spectroscopy data (in $CDCl_3$ solution); $^{31}P\{^1H\}$ NMR -83.4ppm, s, $^1J_{PH}$ = 203 Hz); $^1H$ NMR 1.85 ppm (m, $PCH_2CH_2$), 1.65 ppm (m, $PCH_2$), 2.89 ppm (m, PH); $^{13}C\{^1H\}$NMR 24.4 ppm (s, $PCH_2CH_2$) 18.9 ppm (dd. PCH $^1J_{PC}$ = 11 Hz, $^3J_{PC}$ = 8 Hz). IR spectroscopy (selected): 2277 $cm^{-1}$ ($V_{(PH)}$). Mass spectrum: 221 amu ($M^+$).

EXAMPLE 11

Preparation of 1,5,9-tris(methoxypropene)triphosphacyclododecane [*cyclo*-$\{MeOCH_2CH_2CH_2\}_3PC_3H_6)_3$] (31)

To a solution of [$Cr(CO)_3$cyclo-$\{MeOCH_2CH_2CH_2\}_3PC_3H_6)_3$] 2.0 g, 3.5 mmol) in $CH_2Cl_2$ (50 $cm^3$) was passed $Cl_2$ gas over a period of 5 minutes until the blue-violet colour appeared. The reaction mixture was stirred for a further 4 hours, and the solvent was removed *in vacuo* to give a blue solid, which was washed with light petroleum and recrystallised from $CH_2Cl_2$ affording [$CrCl_3$cyclo-$\{MeOCH_2CH_2CH_2\}_3PC_3H_6)_3$] as blue prisms (1.79 g, 86%).

A suspension of [$CrCl_3$cyclo-$\{MeOCH_2CH_2CH_2\}_3PC_3H_6)_3$] (1.79 g, 3 mmol) in ethanol (30 $cm^3$) was cooled to 0°C and a large excess of NaOH pellets (>1.0 g) added. The mixture was allowed to warm to room temperature and stirred for a further 4 hours. The solvent was removed *in vacuo* to give an oily grey residue. The mixture was cooled to 0°C, $H_20$ (30 $cm^3$) added, and the mixture allowed to warm to room temperature and stirred (1 hour). The product was extracted into petroleum ether (b.p. 40-60°C, 3 x 50 $cm^3$). The combined organic phases were dried ($MgSO_4$, 8 hours), filtered, and the solvent removed *in vacuo* to give (31) as a white, waxy solid (1.04 g, 2.4 mmol, 80% based on chromiumtrichloride) which was soluble in all common organic solvents and may be crystallised from aliphatic hydrocarbons. The macrocycle was liberated in similar yields from the analogous bromo complex using the same method.

NMR spectroscopic data (in $CDCl_3$ solution); $^{31}P\{^1H\}$ NMR - 39.5 p.p.m.(s); 1H NMR 3.34 ppm (t, $^2J_{HH}$=7 Hz) $OCH_2CH_2CH_2$, 3.26 ppm(s) $OCH_3$1.69(m) $PCH_2CH_2CH_2$, 1.58 ppm (q, $^3J_{HH}=^2J_{PH}$=8 Hz) $PCH_2CH_2CH_2O$, 1.35 ppm(m,br)$PCH_2CH_2CH_2P$, $PCH_2CH_2CH_2O$; $^{13}C\{^1H\}$ NMR 73.4 ppm(d, $^3J_{CP}$=13 Hz) $OCH_2CH_2CH_2$, 58.4 ppm(s)

$OCH_3$, 29.5 ppm (d, $^1J_{CP}$=14 Hz) $PCH_2CH_2CH_2O$, 27.1 ppm (dd, $^1J_{CP}$=14 Hz, $^3J_{CP}$=9 Hz) $PCH_2CH_2CH_2$, 23.2(d, $^2J_{CP}$=7 Hz) $PCH_2CH_2CH_2O$, 19.2 ppm (t, $^2J_{CP}$= 7 Hz) $PCH_2CH_2CH_2P$. Mass spec data (selected); 438 ($M^+$ 20%), 365 {$[M-(MeOC_3H_6)]^+$ 100%}. m.p. *ca.* 14°C.

**EXAMPLE 12**

Preparation of 1,5,9-tri(ethoxy-ethene)triphosphacyclododecane [*cyclo*-$\{EtOCH_2CH_2\}_3PC_3H_6)_3$]. (32)

The identical method of example 9 was used but with [$Cr(CO)_3$cyclo-$\{EtOCH_2CH_2\}_3PC_3H_6)_3$] as the starting material.

NMR spectroscopic data (in $CDCl_3$ solution); $^{31}P\{^1H\}$ NMR-42.0 p.p.m.(s); 1H NMR 3.72 ppm (t, $^2J_{HH}$=7 Hz) $OCH_2CH_2$, 3.45 ppm (q, $^2J_{HH}$=7 Hz) $OCH_2CH_3$, 1.90 ppm (m,br) $PCH_2CH_2O$, 1.65 ppm(m) $PCH_2CH_2$, 1.46 ppm(m) $PCH_2CH_2$, 1.10 (t, $^2J_{HH}$=7 Hz) $OCH_2CH_3$; $^{13}C\{^1H\}$ NMR 65.2 ppm(s) $OCH_2CH_2$, 64.1 ppm(s) $OCH_2CH_3$, 32.8 ppm(cm) $OCH_2CH_2$, 27.5 ppm (dd, $^1J_{CP}$=14 Hz, $^3J_{CP}$=9 Hz) $PCH_2CH_2$, 18.4 ppm(cm) $PCH_2CH_2$, 14.0 ppm(s) $OCH_2CH_3$. Mass spec data (selected); 438 ($M^+$ 30%), 365 {$[M-(MeOC_3H_6)]^+$ 100%}. m.p. *ca.* 16°C.

**EXAMPLE 13**

Preparation of syn, anti-1,5,9-trimethyl 1,5,9-triphosphacyclododecane [*cyclo*-$\{(CH_3PC_3H_6)_3$]. (33)

To a cooled (-78°C) solution of 1,5,9-triphosphacyclododecane (0.30 mmol) in tetrahydrofuran (thf)(20 $cm^3$) was added a solution of *n*-BuLi (0.9 mmol) in hexane (1 $cm^3$) dropwise and the mixture allowed to warm slowly to -20°C. The mixture was then recooled to -78°C and RX [0.90 mmol, MeI was added dropwise. The mixture was allowed to warm slowly to room temperature and then stirred for 30 minutes. The solvent was removed

in *vacuo* to give a pale coloured oil that was dissolved in $CH_2Cl_2$ (30 $cm^3$), and passed through a short silica column (5 cm) with $CH_2Cl_2$ as eluant. Evaporation *in vacuo* gave the desired product which was then recrystallised from petroleum ether at -20°C (yield: 80-90%).

NMR spectroscopic data (in $CDCl_3$ solution); $^{31}P\{^1H\}$ NMR- 38.3 (t) -49.5 (d) p.p.m. ($^4J_{PP}$=39 Hz); 1H NMR 1.82 ppm (m) $PCH_2CH_2$, 1.63 ppm (m) $PCH_2CH_2$, 0.98 ppm (s,br) $PCH_3$, $^{13}C\{^1H\}$ NMR 25.5 ppm (m,br) $PCH_2CH_2$, 18.9 ppm (m,br) $PCH_2CH_2$, 8.6 ppm (d, $^1J_{PC}$=16 Hz) $PCH_3$. IR (neat thin film): 2966s, 2924s, 2854m, 1447m, 1412m, 1264(sh), 1096s, 1026s, 700s, 684m, 654m. Mass spec data (selected); 264 ($M^+$ 5%), 219 {$[M-(Me_3)]^+$ 100%}.

**EXAMPLE 14**

Preparation of syn, anti-1,5,9-tri(teriarybutyl)1,5,9-triphosphacyclododecane [*cyclo*-{$(^tBuPC_3H_6)_3$]. **(34)**

The identical method of example 11 was used but with tertiary-butylchloride as the starting material.

NMR spectroscopic data (in $CDCl_3$ solution); $^{31}P\{^1H\}$ NMR- 9.9 (t) -15.7 (d) ppm. ($^4J_{PP}$=40 Hz). $^1H$ NMR 1.79 ppm (m,br) $PCH_2CH_2$, 1.5 ppm (m) $PCH_2CH_2$, 0.98 ppm (s,br) $PCCH_3$, $^{13}C\{^1H\}$ NMR 28.7 ppm (m) $PCH_2CH_2$, 24.6 ppm (d, $^1J_{PC}$=18 Hz) $PCCH_3$, 22.8 ppm (m) $PCH_2CH_2$, 13.9 ppm (d, $^2J_{PC}$= 7 Hz) $PCCH_3$. IR (neat thin film): 2968s, 2928s, 2862m, 1478m, 1422m, 1412m, 1257(sh), 1096s, 1026m, 864m, 801s, 700 s, 684m, 658m. Mass spec data (selected); 390 ($M^+$ 8%), 219 {$[M-(^tBu)_3]^+$ 60%}.

**EXAMPLE 15**

Preparation of syn, anti-1,5,9-tri(ethyl)1,5,9-triphosphacyclododecane [*cyclo*-{$(EtPC_3H_6)_3$]. **(35)**

A solution of $H_3L$ (0.30 mmol) and aibn

(azobisisobutyronitrile)(*ca.* 1%) in toluene (20 $cm^3$) was frozen at -196°C in a glass pressure reaction flask. A large excess of $C_2H_4$ (>1.0 g) was added and the mixture heated at 80°C for 3 hours. The mixture was allowed to cool to room temperature and then filtered through a short celite column (4 cm) to give a colourless solution. The solvent was removed *in vacuo*, and the product obtained as a colourless oil from petroleum ether solution at -20°C (yield: 80%).

NMR spectroscopic data (in $CDCl_3$ solution); $^{31}P\{^1H\}$ NMR -29.4 (t) -38.7 (d) ppm ($^4J_{PP}$=37 Hz). $^1H$ NMR 1.77 ppm (m) $PCH_2CH_2$, 1.49 ppm (m) $PCH_2CH_3$, 1.34 ppm (m) $PCH_2CH_2$, 1.06 ppm (m) P $CH_2CH_3$. $^{13}C\{^1H\}$ NMR 27.6 ppm (m) $PCH_2CH_2$, 19.2 ppm (m) $PCH_2CH_2$, 19.0 ppm (d, $^2J_{PC}$=10 Hz) $PCH_2CH_3$, 10.0 ppm (d, $^1J_{PC}$=16 Hz) P $CH_2CH_3$. IR (neat thin film): 2968s, 2922s, 2860m, 1458m, 1422m, 1356m, 1260(sh), 1096s, 1026s, 864(br), 799s, 700(br).

**EXAMPLE 16**

METAL COMPLEXES OF TRIPHOSPHA MACROCYCLES

1. Preparation of [*cyclo*-(1,5,9-tris(2-propyl)triphosphacyclododecane) rhodium (III) trichloride, [*cyclo*-$(\{CH_3\}_2CHPC_3H_6)_3RhCl_3$]. **(36)**

A solution of *cyclo*-(1,5,9-tris(2-propyl)triphosphacyclododecane) (0.14 mmol) in ethanol (30$cm^3$) was added dropwise to a solution of $RhCl_3.3H_2O$ (0.14 mmol) in ethanol (15 $cm^3$) at room temperature. The mixture was stirred for 1h and solvent removed *in vacuo* to give a pale orange residue. dichloromethane (50 $cm^3$) was added and the mixture filtered through celite to give a pale orange solution. Solvent was removed *in vacuo* and the residue recrystallised from dichloromethane/diethyl ether to give **(36)** as very pale orange prisms (0.10 mmol, 70%).

NMR spectroscopy data; $^{31}P\{^{1}H\}$ NMR 15.6 ppm (d, $^{1}J_{RhP}$106 Hz); $^{1}H$ NMR 1.80 ppm (br m, $PCH_2CH_2$), 1.50 ppm (br m, $PCH$ & $PCH_2$), 1.00 ppm (dd, $^{3}J_{PH}$ 12 Hz & $^{1}J_{HH}$ 9 Hz, $CH_3$). Mass Spec data (selected); 558 ($M^+$, 5%), 533 ($M-Cl^+$, 12%), 497 ($M-Cl_2^+$, 5%), 460 ($M-Cl_3^+$, 5%). Elemental Analysis, % found (% theory); C 38.45 (38.74), H 7.92 (6.99).

2. Preparation of [*cyclo*-(1,5,9-tris(2-propyl)triphosphacyclododecane) rhodium (III) trihydride, [*cyclo*-$(\{CH_3\}_2CHPC_3H_6)_3RhH_3$]. **(37)**

$NaBH_4$ (1.0 mmol, excess) was added to a suspension of **(36)** (0.10 mmol) in ethanol (10 $cm^3$) and stirred at room temperature until effervescence had ceased. Solvent was removed *in vacuo* to give a grey residue. Toluene (20 $cm^3$) was added and the mixture filtered through Celite to give a pale yellow solution. Solvent was removed *in vacuo* to give **(37)** as a pale yellow (60%).

NMR spectroscopy data (in $C_6D_6$); $^{31}P\{^{1}H\}$ NMR 29.6 ppm (d, $^{1}J_{RhP}$ 90 Hz); $^{1}H$ NMR 1.82 ppm (br m, $PCH_2CH_2$), 1.51 ppm (br m, $PCH$ & $PCH_2$), 0.97 ppm (dd, $^{3}J_{PH}$ 12 Hz & $^{1}J_{HH}$ 9 Hz, $CH_3$) -9.42 ppm (ddt, $^{1}J_{RhP}$ 127 Hz). Mass Spec data (selected); 452 ($M^+$, 40%). Infra-red spectroscopy (selected); $\upsilon$(RhH) 1910(s), 1820(s).

3. Preparation of [*cyclo*-(1,5,9-tris(2-propyl)triphosphacyclododecane) rhodium (III) triiodide, [cyclo-$(\{CH_3\}_2CHPC_3H_6)_3RhI_3$]. **(38)**

A suspension of **(37)** (0.10 mmol) in MeI (10 $cm^3$) was stirred at room temperature for 48h. The mixture was allowed to settle and the supernatant solution removed by filtration to give **(38)** as an orange solid which was then washed with diethyl ether (2 x 10$cm^3$) (0.08 mmol, 78%).

NMR spectroscopy (selected); $^{31}P\{^{1}H\}$ NMR -1.38 ppm (d,

$^{1}J_{RhP}$ 106 Hz). Elemental Analysis, % found (% theory); C 25.72 (25.96), H 5.20 (4.69).

4. Preparation of [*cyclo*-(1,5,9-tris(trimethylsilylmethyl)triphosphacyclododecane) rhodium (III) trichloride, [*cyclo*-$(\{CH_3\}_3SiCH_2PC_3H_6)_3RhCl_3$]. **(39)**

The same method was employed as for **(36)** but using 1,5,9-*cyclo*-tris(trimethylsilylmethyl)triphosphacyclododecane as starting material.

$^{31}P\{^{1}H\}$ NMR spectroscopy; 19.4 ppm (d, $^{1}J_{RhP}$ 109 Hz).

5. Preparation of [*cyclo*-(1,5,9-tri(2-propyl)triphosphacyclododecane) rhodium (I) chloride, [*cyclo*-$(\{CH_3\}_2CHPC_3H_6)_3RhCl$]. **(40)**

A solution of *cyclo*-(1,5,9-tris(2-propyl)triphosphacyclododecane) (0.10 mmol) in petroleum ether (20 $cm^3$) was added to a suspension of $[RhCl(C_8H_{14})_2]_2$ (0.05 mmol) in petroleum ether (20 $cm^3$) and the mixture stirred at room temperature for 1h. The mixture was allowed to settle and the supernatant solution removed by filtration. The resultant residue was washed with petroleum ether (20 $cm^3$) to give **(40)** as a yellow solid (0.06 mmol, 58%).

Elemental Analysis, % found (% theory); C 45.08 (44.40), 8.45 (8.02).

6. Preparation of [*cyclo*-(1,5,9-tris(2-propyl)triphosphacyclododecane) cyclopentadienyl iron (II) hexafluorophosphate, [*cyclo*-$(\{CH_3\}_2CHPC_3H_6)_3(C_5H_5)Fe]PF_6$. **(41)**

A solution of *cyclo*-(1,5,9-tris(2-

propyl)triphosphacyclododecane) (0.10 mmol) in thf (20 $cm^{3)}$ was added to a solution of $[Fe(C_5H_5)(C_6H_6)]PF_6$ (0.10 mmol) in thf (30 $cm^3$) and the mixture irradiated under UV radiation for 8h. Solvent was removed *in vacuo* and the resultant yellow residue recrystallised from dichloromethane/petroleum ether 40-60°C to give **(41)** as a yellow solid (0.07 mmol, 72%).

NMR spectroscopy (in CD3OD); $^{31}P\{^1H\}$ NMR 37.0 ppm (s); $^1H$ NMR 4.34 ppm (q, $^3J_{PH}$ 2 Hz, $C_5H_5$); 1.85 ppm (br m, $PCH_2CH_2$), 1.60 ppm (br m, PCH & $PCH_2$), 1.18 ppm (dd, $^3J_{PH}$ 13 Hz & $^1J_{HH}$ 7 Hz, $CH_3$). $^{13}C\{^1H\}$ NMR 77.5 ppm (s, $C_5H_5$), 32.4 (br m, $PCH_2$), 21.7 ppm (m, $PCH_2CH_2$), 18.6 ppm (m, PCH), 17.8 (s, $CH_3$).

Elemental Analysis, % found (% theory); C 44.18 (44.98); H 6.89 (7.17).

7. Preparation of [*cyclo*-(1,5,9-tris(2-propyl)triphosphacyclododecane) cyclopentadienyl ruthenium (II) hexafluorophosphate, [*cyclo*-$(\{CH_3\}_2CHPC_3H_6)_3(C_5H_5)Ru]PF_6$. **(42)**

A solution of *cyclo*-(1,5,9-tris(2-propyl)triphosphacyclododecane) (0.10 mmol) in dichloromethane (30 $cm^3$) was added dropwise to a solution of $[Ru(C_5H_5)CH_3CN)_3]PF_6$ (0.10 mmol) in dichloromethane (30 $cm^3$) and the mixture stirred at room temperature for 1h. Solvent was removed *in vacuo* and recrystallisation from dichloromethane/petroleum ether 40-60°C gave **(43)** as yellow prisms (0.04 mmol, 39%).

$^{31}p\{^1H\}$ NMR spectroscopy; 23.7 ppm (s).

8. Preparation of [*cyclo*-(1,5,9-tri(2-propyl)triphosphacyclododecane) ruthenium (II) dichloride, [*cyclo*-$(\{CH_3\}_2CHPC_3H_6)_3RuCl_2]$. **(43)**

A solution of *cyclo*-(1,5,9-tris(2-propyl)triphosphacyclododecane) (0.10 mmol) in dichloromethane (10 $cm^3$) was added to a suspension of $[RuCl_2(\{CH_3\}_2SO)_4]$ (0.10 mmol) in dichloromethane (30$cm^3$). The mixture was stirred at room temperature for 1h and then filtered through Celite to give a bright yellow solution. Solvent was removed *in vacuo* and recrystallisation from dichloromethane/petroleum ether 40-60°C gave **(43)** as a yellow solid (0.07 mmol, 68%).

$^{31}P\{^1H\}$ NMR spectroscopy; 33.9 ppm (s).

9. Preparation of [*cyclo*-(1,5,9-tris(2-propyl)triphosphacyclododecane) copper (I) bromide, [*cyclo*-$(\{CH_3\}_2CHPC_3H_6)_3(C_5H_5)CuBr$]. **(44)**

A solution of *cyclo*-(1,5,9-tris(2-propyl)triphosphacyclododecane) (0.10 mmol) in dichloromethane (10 $cm^3$) was added to CuBr (0.10 mmol) and the mixture stirred for 4h. Solvent was removed *in vacuo* and recrystallisation from dichloromethane/petroleum ether 40-60°C gave (45) as a yellow solid (0.08 mmol, 78%).

$^{31}P\{^1H\}$ NMR spectroscopy; -23.8 ppm (s).

10. Preparation of [*cyclo*-(1,5,9-tris(2-propyl)triphosphacyclododecane)(L) ruthenium (II) dichloride, [*cyclo*-$(\{CH_3\}_2CHPC_3H_6)_3(L)RuCl_2$] (L = Triphenylphosphine **(45)**, dimethylphenylphosphine. **(46)**

A solution of *cyclo*-(1,5,9-tris(2-propyl)triphosphacyclododecane) (0.10 mmol) in toluene (20 $cm^3$) was added to $RuCl_2(L)_4$ (0.10 mmol; L = $PPh_3$, $PMe_2Ph$) and the mixture heated to reflux temperature for 16h. The mixture was allowed to cool to room temperature and then filtered through Celite. Solvent was removed *in*

*vacuo* and recrystallisation from toluene/petroleum ether 40-60°C gave **(45)** as a red/brown solid (65%) or **(46)** as a white solid (51%).

11. Preparation of [(*cyclo*-1,5,9-triphosphacyclododecane) copper (1) bromide]. **(47)**

To a suspension of CuBr (0.25 g, 1.8 mmol) in $CH_2Cl_2$ (25 $cm^{-3}$), was added H3L (0.4 g, 1.8 mmol) at room temperature and the mixture stirred (4 hours) during which time the CuBr had dissolved. The resultant clear solution was evaporated to dryness *in vacuo* leaving a white solid which was washed with light petroleum (2 x 10 $cm^{-3}$). Yield = 0.5 g, 75%; Analysis, found (calc.), C%, 28.25 (29.5); H%, 5,90 (5.75); $\delta_p$ ($CDCl_3$, 36.23 MHZ) -73.0 (d, $J_{PH}$=307 Hz); $\delta_H$ ($CDCl_3$, 360.13 MHZ), 4.4 (P*H*), 2.07 ($PCH_2CH_2$), 1.54 ($PCH_2CH_2$); $\delta_C$ ($CDCl_3$, 22.49 MHZ) 24.3 (m, $PCH_2CH_2$), 21.2 (m, $PCH_2CH_2$); *m/z* 365.5 ($M^+$, 10%), 222 ((M-CuBr)$^+$, 100%.

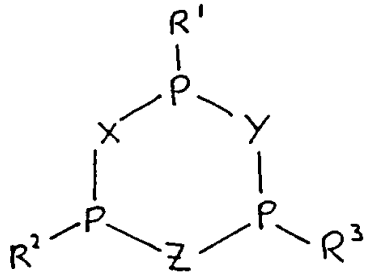
12. Preparation of carbonyl *cyclo*-(1,5,9-tris(ethyl)triphosphacyclododecane) nickel nitrate $[LNi(CO)]^+NO_3$. **(48)**

To a solution of $Ni(NO_3)_2$ in ethanol was added L (L = 1,5,9-triethyl-1,5,9-triphophacyclododecane) (1 mole equivalent) and CO gas bubbled through the solution. The reaction mixture was stirred (2h) and then evaporated to dryness. The residue was extracted into chloroform, concentrated, and the product crystallised by cooling (-20°C).

CLAIMS:

1. A process for the preparation of a compound of formula (I):

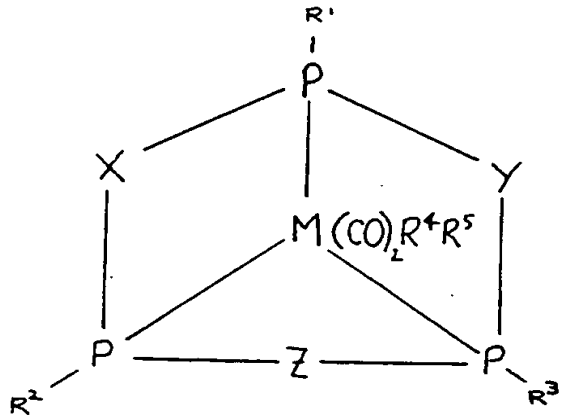
(I)



where $R^1$, $R^2$ and $R^3$ may be the same or different and are hydrogen, or optionally substituted hydrocarbyl or optionally substituted heterocyclyl groups; and X, Y and Z may be the same or different and are optionally substituted alkylene or arylene groups; which process comprises either:

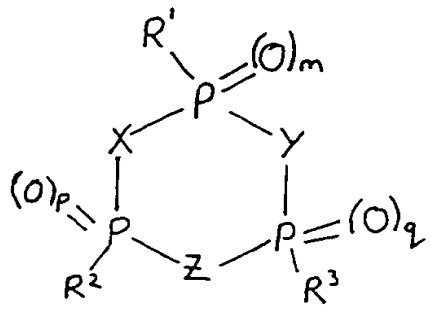
(a) reacting a compound of formula (II):

(II)



where $R^1$ , $R^2$ , $R^3$, X, Y and Z are as defined above, M is a metal, $R^4$ is halogen and $R^5$ is hydrogen or halogen, with a base, or optionally a metal scavenging agent such as EDTA or cyanides; or:

(b) reducing a compound of formula (III):

(III) 

where $R^1$ , $R^2$ , $R^3$, X, Y and Z are as defined above, and m, p and q are 0 or 1 provided that at least one of m, p or q is 1;

and optionally thereafter changing one or more of the groups $R^1$, $R^2$ and $R^3$ for other such groups.

2. A process according to claim 1 wherein $R^1$, $R^2$ and $R^3$ may be the same or different and are hydrogen or optionally substituted alkyl.

3. A process according to claim 2 wherein $R^1$, $R^2$ and $R^3$ are all hydrogen or all alkyl.

4. A process according to any one of the preceding claims wherein X, Y and Z may be the same or different and are optionally substituted trimethylene, tetramethylene or 1,2-phenylene.

5. A process according to any one of the preceding claims wherein the metal M is a transition metal.

6. A process according to claim 5 wherein the metal M is chromium, molybdenum or tungsten.

7. A process according to any one of the preceding claims wherein $R^4$ and $R^5$ are chlorine.

8. A process according to any one of the preceding claims wherein the base for use in reaction (a) is an alkali metal hydroxide or alkoxide.

9. A process according to claim 8 wherein the base is sodium hydroxide.

10. A process according to any one of the preceding claims wherein reaction (a) is carried out in an aqueous or alcoholic solvent or mixture thereof.

11. A process according to any one of the preceding claims wherein reaction (a) is carried out at a temperature range of from 0°C to 100°C.

12. A process according to any one of claims 1-4, wherein the compound of formula (III) is reduced with lithium aluminium hydride or trichlorosilane.

13. A compound of formula (I) as defined in claim 1.

14. A compound according to claim 13 wherein all three lone pairs of electrons on the phosphorus atoms are orientated on the same side of the ring structure.

15. A compound according to claim 13 or claim 14 wherein $R^1$, $R^2$ and $R^3$ are the same or different and are hydrogen or optionally substituted alkyl.

16. A compound according to claim 15 wherein $R^1$, $R^2$ and $R^3$ are all hydrogen or all alkyl.

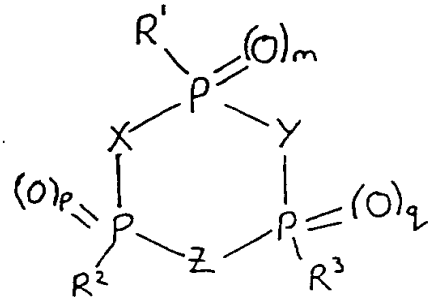
17. A compound according to any one of claims 13 to 16 wherein X, Y and Z may be the same or different and

are optionally substituted trimethylene, tetramethylene or 1,2-phenylene.

18. A compound according to any one of claims 13 to 17 wherein X, Y and Z are the same.

19. A compound of formula (III):

(III)



where $R^1$, $R^2$, $R^3$, may be the same or different and are hydrogen, or optionally substituted hydrocarbyl or optionally substituted heterocyclyl groups; and X, Y and Z may be the same or different and are optionally substituted alkylene or arylene groups and where m, p, q are 0 or 1 provided at least one of m, p or q is 1.

20. A compound according to claim 19 wherein $R^1$, $R^2$ and $R^3$ may be the same or different and are hydrogen or optionally substituted alkyl.

21. A compound according to claim 20 wherein $R^1$, $R^2$ and $R^3$ are all hydrogen or all alkyl.

22. A compound according to any one of claims 19 to 21 wherein X, Y and Z may be the same or different and are optionally substituted trimethylene, tetramethylene or 1,2-phenylene.

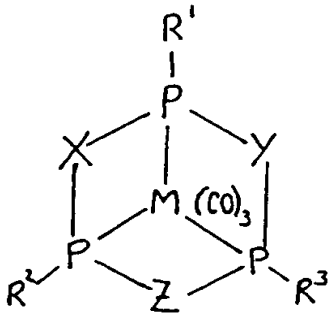
23. A compound according to claim 19 wherein X, Y and Z are the same.

24. A process for the preparation of a compound of formula

(III) as defined in claim 19 comprising:

oxidizing a compound of formula (V):

(V)




where $R^1$, $R^2$, $R^3$ may be the same or different and are hydrogen, or optionally substituted hydrocarbyl or optionally substituted heterocyclyl groups; and X, Y and Z may be the same or different and are optionally substituted alkylene or arylene groups and M is a transition metal; using an oxidizing agent.

25. A process according to claim 24 wherein the oxidizing agent is either hydrogen peroxide, oxygen or ozone.

26. A process according to claim 24 or claim 25 wherein the reaction takes place in an organic solvent.

27. A process according to any one of claims 24 to 26 wherein the reaction is carried out at a temperature between 0°C and 100°C.

28. A process according to any one of claims 24 to 27 wherein M is Chromium.

29. A catalyst comprising a metal complex of a compound as defined in claim 13 or claim 19 or a metal complex, other than a molybdenum complex, of a compound of formula (I) as defined in claim 1.

30. Use of a metal complex of a compound as defined in claim 13 or claim 19 or a metal complex, other than a

molybdenum complex, of a compound of formula (I) as defined in claim 1 as a catalyst.

# INTERNATIONAL SEARCH REPORT

International Application No
GB 96/01943

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07F9/6568 C07F15/00 C07F11/00 B01J31/22

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07F B01J

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | BULL. KOREAN CHEM. SOC. (BKCSDE,02532964);94; VOL.15 (5); PP.331-2, GYEONGSANG NATL. UNIV.;DEP. CHEM. EDU.; CHINJU; 660-701; S. KOREA (KR), XP000607405<br>KIM B G ET AL: "A facile synthesis of triphosphine macrocycles [12]aneP3R3 (R = H, CH3) by template reaction"<br>see the whole document<br>---<br>-/-- | 1-6, 8-11,13, 15-18 |

[X] Further documents are listed in the continuation of box C.

[ ] Patent family members are listed in annex.

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1

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 11 November 1996 | 28. 11. 96 |

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Form PCT/ISA/210 (second sheet) (July 1992)

International Application No
PCT/GB 96/01943

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | INORG. CHEM. (INOCAJ,00201669);85; VOL.24 (11); PP.1613-16, UNIV. TEXAS;DEP. CHEM.; AUSTIN; 78712; TX; USA (US), XP000607427 KYBA E P ET AL: "Phosphino macrocycles***. 140. Synthesis of unusual phosphine ligands. Use of the 1-naphthylmethyl moiety as a P-H protecting group in the synthesis of a phosphino macrocycle that contains a secondary-phosphino ligating site" see the whole document | 1-4,12 |
| X | JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 99, no. 24, 1977, DC US, pages 8053-8054, XP000608358 EVAN P. KYBA: "Polyphosphino Macrocyclic Ligand Systems" cited in the application see formulas 7 and 8 | 1,17 |
| A | J. CHEM. SOC., DALTON TRANS. (JCDTBI,03009246);95; (7); PP.1139-45, UNIV. WALES;DEP. CHEM.; CARDIFF; CF1 3TB; UK (GB), XP002018125 COLES S J ET AL: "1,5,9-Triphosphacyclododecane complexes of molybdenum and tungsten. Crystal structure of tricarbonyl[1,5,9-tris(isopropyl)-1,5,9-triphosp hacyclododecane]molybdenum(0)" cited in the application see the whole document | 1-28 |
| A | J. AM. CHEM. SOC. (JACSAT,00027863);82; VOL.104 (17); PP.4700-1, UNIV. COLORADO;DEP. CHEM.; BOULDER; 80309; CO; USA (US), XP000608359 DIEL B N ET AL: "Metal-templated synthesis of a macrocyclic*** triphosphine-molybdenum complex, fac-(CO)3Mo(PHC3H6)3" see the whole document | 1-28 |
| P,X | INORG. CHEM. (INOCAJ,00201669);96; VOL.35 (16); PP.4563-4568, UNIVERSITY OF WALES CARDIFF;DEPARTMENT OF CHEMISTRY; CARDIFF; CF1 3TB; UK (GB), XP000607383 EDWARDS P G ET AL: "Stereoselective Synthesis of 1,5,9-Triphosphacyclododecane and Tertiary Derivatives" see the whole document | 1-30 |

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| P,X | J. CHEM. SOC., DALTON TRANS. (JCDTBI,03009246);96; (9); PP.1801-1807, UNIV. WALES;DEP. CHEM.; CARDIFF; CF1 3TB; UK (GB), XP000608171<br>EDWARDS P G ET AL: "Primary alkenyl phosphine complexes of chromium and molybdenum;synthesis and characterization of tricarbonyl(1,5,9-triphosphacyclodo decane)chromium(0)"<br>see the whole document<br>--- | 1-30 |
| P,X | CHEM. COMMUN. (CAMBRIDGE) (CHCOFS,13597345);96; (3); PP.293-4, UNIV. WALES;DEP. CHEM.; CARDIFF; CF1 3TB; UK (GB), XP000608172<br>COLES S J ET AL: "The liberation, characterization and x-ray crystal structure of 1,5,9-triphospha-1,5,9-tris(2-propyl)cyclo dodecane"<br>see the whole document<br>----- | 1-30 |

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(71) Applicant *(for all designated States except US)*: UNIVERSITY COLLEGE CARDIFF CONSULTANTS LIMITED [GB/GB]; P.O. Box 923, Cardiff CF1 3TE (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: EDWARDS, Peter, Gerald [GB/GB]; 81 Plymouth Road, Penarth, South Glamorgan CF64 3DE (GB). FLEMING, James, Stephen [GB/GB]; University College Cardiff Consultants Limited, P.O. Box 923, Cardiff CF1 3TE (GB). LIYANNAGE, Sudantha, Susila, Lekam, Wasam [LK/GB]; University College Cardiff Consultants Limited, P.O. Box 923, Cardiff CF1 3TE (GB).

(74) Agents: STUART, Ian et al.; Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP (GB).

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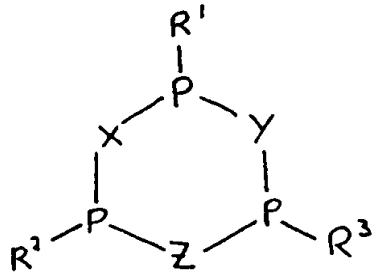
(54) Title: CYCLIC PHOSPHINES, PHOSPHINE OXIDES AND COMPLEXES THEREOF

(57) Abstract

The invention relates to processes for the preparation of phosphine derivatives, to certain novel phosphine derivatives obtainable by this process and to their uses, for example in catalysis. In particular, to a process for the preparation of a compound of formula (I) where $R^1$, $R^2$ and $R^3$ may be the same or different and are hydrogen, or optionally substituted hydrocarbyl or optionally substituted heterocyclyl groups; and X, Y and Z may be the same or different and are optionally substituted alkylene or arylene groups.

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